

10/537741
JC17 Rec'd PCT/PTO 03 JUN 2005

In the Claims:

The claims and their status are shown below.

1. (Original) An isolated antisense oligonucleotide consisting essentially of 10 to 50 nucleotides, wherein said oligonucleotide specifically hybridizes within an accessible region, said region defined by nucleotides 4276 through 4294, 3879 through 3896, 5661 through 5678, or 2821 through 2838 of SEQ ID NO:1, and wherein said oligonucleotide inhibits the production of TRPM2.
2. (Original) A composition comprising the isolated antisense oligonucleotide of claim 1.
3. (Original) The composition of claim 2, wherein said composition comprises a plurality of isolated antisense oligonucleotides, wherein each antisense oligonucleotide specifically hybridizes within a different accessible region.
4. (Original) The isolated antisense oligonucleotide of claim 1, wherein said oligonucleotide comprises a modified backbone.
5. (Original) The isolated antisense oligonucleotide of claim 1, wherein said oligonucleotide comprises one or more non-natural internucleoside linkages.
6. (Original) The isolated antisense oligonucleotide of claim 1, wherein said oligonucleotide is an oligonucleotide analog.
7. (Original) The isolated antisense oligonucleotide of claim 1, wherein said oligonucleotide comprises one or more substituted sugar moieties.

8. (Original) The isolated antisense oligonucleotide of claim 1, wherein said oligonucleotide comprises nucleotide base modifications or nucleotide base substitutions.

9. (Original) An isolated antisense oligonucleotide consisting essentially of 10 to 50 nucleotides, wherein said oligonucleotide specifically hybridizes within an accessible region, said region defined by nucleotides 273 through 294, 1848 through 1878, 3759 through 3782, 481 through 501, 1971 through 1988, 2067 through 2084, 2165 through 2187, 4139 through 4161, or 4248 through 4270 of SEQ ID NO:2, and wherein said isolated antisense oligonucleotide inhibits the production of TRPM2.

10. (Original) A composition comprising the isolated antisense oligonucleotide of claim 9.

11. (Original) The composition of claim 10, wherein said composition comprises a plurality of isolated antisense oligonucleotides, wherein each antisense oligonucleotide specifically hybridizes with a different accessible region.

12. (Original) An isolated oligonucleotide consisting essentially of the sequence of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; SEQ ID NO:13; SEQ ID NO:14; or SEQ ID NO:15.

13. (Original) A method of decreasing production of TRPM2 in cells or tissues, comprising contacting said cells or tissues with an antisense oligonucleotide that specifically hybridizes within an accessible region of TRPM2.

14. (Original) The method of claim 13, wherein said contacting step results in an inhibition of pain sensory neurons.

15. (Original) A nucleic acid construct comprising a regulatory element operably linked to a nucleic acid encoding a transcript, wherein said transcript specifically hybridizes within one or more accessible regions of TRPM2 mRNA in its native form.

16. (Original) A host cell comprising the nucleic acid construct of claim 15.

17. (Original) An isolated antisense oligonucleotide that specifically hybridizes within an accessible region of TRPM2 mRNA in its native form, and wherein said antisense oligonucleotide inhibits production of TRPM2.

18. (Original) A method for modulating pain in a mammal, said method comprising administering the isolated antisense oligonucleotide of claim 17 to said mammal.

19. (Original) A method of identifying a compound that modulates pain in a mammal, the method comprising:

contacting cells comprising a TRPM2 nucleic acid with a compound; and
detecting the amount of TRPM2 RNA or TRPM2 polypeptide in or secreted from said cell,

wherein a difference in the amount of TRPM2 RNA or TRPM2 polypeptide produced in the presence of said compound compared to the amount of TRPM2 RNA or TRPM2 polypeptide produced in the absence of said compound is an indication that said compound modulates pain in said mammal.

20. (Original) The method of claim 19, wherein the amount of said TRPM2 RNA is determined by Northern blotting.

21. (Original) The method of claim 19, wherein the amount of said TRPM2 polypeptide is determined by Western blotting.
22. (Original) The method of claim 19, wherein said compound is an antisense oligonucleotide that specifically hybridizes within an accessible region of TRPM2 mRNA in its native form, wherein said antisense oligonucleotide inhibits production of TRPM2.
23. (Original) A method of identifying a compound that modulates pain in a mammal, the method comprising:
 contacting cells comprising a TRPM2 nucleic acid with a compound; and
 detecting the activity of TRPM2 in or secreted from said cell,
 wherein a difference in the activity of TRPM2 in the presence of said compound compared to the activity of TRPM2 in the absence of said compound is an indication that said compound modulates pain in said mammal.
24. (Original) A method for modulating pain in a mammal, said method comprising administering a compound to said mammal, wherein said compound modulates the expression of TRPM2.
25. (Original) The method of claim 24, wherein said compound is an antisense oligonucleotide that specifically hybridizes within an accessible region of TRPM2 mRNA in its native form, wherein said antisense oligonucleotide inhibits expression of TRPM2.
26. (Original) The method of claim 24, wherein said pain is from diabetic neuropathy, gastric pain, postherpetic neuralgia, fibromyalgia, surgery, or chronic back pain.

27. (Original) A method for modulating pain in a mammal, said method comprising administering a compound to said mammal, wherein said compound modulates the function of TRPM2.

28. (Original) The method of claim 27, wherein said pain is from diabetic neuropathy, gastric pain, postherpetic neuralgia, fibromyalgia, surgery, or chronic back pain.